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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/827,846	04/06/2001	Shinichi Eda	RDC 12320 Div.	7993

26345 7590 01/23/2004

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EXAMINER	
GABEL, GAILENE	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 01/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/827,846	EDA ET AL.	
	Examin r	Art Unit	
	Gailene R. Gabel	1641	

--Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 02 December 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *see attached*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: *NONE*.

   Claim(s) objected to: *NONE*.

   Claim(s) rejected: *1-4,6,9,10,20,22 and 23*.

   Claim(s) withdrawn from consideration: *NONE*.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

11/14/04

ADVISORY ACTION

Amendment Entry

1. Applicant's amendment and response filed 12/9/03 is acknowledged and has been entered. Claim 20 has been amended. Currently, claims 1-4, 6, 9, 10, 20, 22, and 23 are pending and are under examination.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2. Claims 1-4, 6, 10, and 20 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Lindmo et al. (Journal of Immunological Methods, 126: 183-189

(1990)) in view of Grange et al. (Journal of Immunological Methods (1977)) for reasons of record.

3. Claim 9 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Lindmo et al. (Journal of Immunological Methods, 126: 183-189 (1990)) in view of Grange et al. (Journal of Immunological Methods (1977)) as applied to claims 1-4, 6, 10, and 20 above, and further in view of Sutton et al. (US Patent 5,330,891) for reasons of record.

4. Claim 22 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Lindmo et al. (Journal of Immunological Methods, 126: 183-189 (1990)) in view of Grange et al. (Journal of Immunological Methods (1977)) as applied to claims 1-4, 6, 10, and 20 above, and further in view of Collet-Cassart et al. (US Patent 4,556,642) for reasons of record.

5. Claim 23 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Lindmo et al. (Journal of Immunological Methods, 126: 183-189 (1990)) in view of Grange et al. (Journal of Immunological Methods (1977)) as applied to claims 1-4, 6, 10, and 20 above, and further in view of Kapmeyer et al. (An automated particle-enhanced nephelometric assay for the quantitative determination of PSA, Clinical Chemistry, (1996) Vol. 42, No. 6 PART 2, pp. S268-S269) for reasons of record.

Response to Arguments

6. Applicant's arguments filed 12/2/03 have been fully considered but they are not persuasive.

A) Applicant argues that Lindmo et al. does not anticipate the claimed invention because it fails to disclose first and second microparticles having a diameter of 30 to 600 nm for measurement at wavelengths of 300 to 1200 nm. Applicant specifically contends that Lindmo et al. discloses differential characterization between two microparticle populations having immunological binding partners in flow cytometry applications; however, it does not teach or suggest agglutination applications which require the particles to be small and colloidal, i.e. 30 nm to 600 nm. Thus, Applicant argues that the teachings of Lindmo et al. are based on principles unrelated to those for which the claimed reagent is suitable for use.

In response to applicant's arguments against the Lindmo et al. reference individually, one cannot show nonobviousness by attacking the reference individually where the rejection is based on a combination of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, Lindmo et al. teach a reagent comprising a binary mixture of microparticles having two distinguishable microparticle types wherein each population has a mean diameter, has distinguishable light scattering properties, i.e. refractive index, and is differentially coated with binding partners having the same specificity but different reactivity. Grange et al. is incorporated with the teaching of Lindmo et al. only for the teaching of a reagent comprising light scattering microparticles having a diameter of 300 nm for measurement at wavelengths of 220 nm to 600 nm suitable for agglutination assays. Thus, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to generate microparticles in the size

range of about 300 nm as taught by Grange, for incorporation into the reagent taught by Lindmo for use in agglutination assay detection methods because Grange specifically taught that intensity of light scatter by a given suspension of microparticles in a reagent, when used in an agglutination assay is dependent on the size, i.e. 300 nm and number of the particles.

Additionally, the claimed invention is drawn to a reagent comprising a mixture of microparticles for use in an agglutination assay. A recitation of the intended use of the claimed reagent must result in a structural difference between the claimed reagent and the prior art (Lindmo in combination with Grange) in order to patentably distinguish the claimed invention from the prior art. Thus, if the prior art structure created by the combined teaching of Lindmo and Grange, is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey,* 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

B) Applicant argues that Grange et al. discloses microparticles having a diameter of 300 nm for agglutination assay measurements at 200 nm to 600 nm; but fails to teach differential characterization between two microparticle populations. Applicant contends that Grange et al. also does not teach differential reactivity and dissociation constants between two immunological binding partners bound to the two microparticle populations. Thus, Applicant argues that the teaching of Grange et al. cannot be combined with the teaching of Lindmo et al. because Lindmo et al. does not

teach agglutination assay applications but rather operates on unrelated and distinct principles which use non-colloidal particles.

In response to applicant's arguments against the Grange et al. reference individually, one cannot show nonobviousness by attacking the reference individually where the rejection is based on a combination of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, Lindmo et al. teach a reagent comprising a binary mixture of microparticles having two distinguishable microparticle types wherein each population has a mean diameter, distinguishable light scattering properties, i.e. refractive index, and are coated with binding partners having the same specificity but different reactivity. Grange et al. is incorporated with the teaching of Lindmo, only for the teaching of a reagent comprising light scattering microparticles having a diameter of 300 nm for measurement at wavelengths of 220 nm to 600 nm. Thus, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to generate microparticles in the size range of about 300 nm as taught by Grange, for incorporation into the reagent taught by Lindmo for use in agglutination assay detection methods because Grange specifically taught that intensity of light scatter by a given suspension of microparticles in a reagent, when used in an agglutination assay is dependent on the size, i.e. 300 nm and number of the particles.

Additionally, the claimed invention is drawn to a reagent comprising a mixture of microparticles for use in an agglutination assay. A recitation of the intended use of the claimed reagent must result in a structural difference between the claimed reagent and

the prior art (Lindmo in combination with Grange) in order to patentably distinguish the claimed invention from the prior art. Thus, if the prior art structure created by the combined teaching of Lindmo and Grange, is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

C) Applicant states that Sutton et al. disclose a microparticulate reagent having an oligonucleotide probe covalently attached thereto and concurs that such teaching is well known in the art. Applicant, however, argues that Sutton et al. fails to remedy the deficiency of the combined teaching of Lindmo et al. and Grange et al. since Lindmo et al. teaches away from the claimed invention for lack of teaching of agglutination assay applications and thus, is not combinable with the teaching of both Grange et al. and Sutton et al. According to Applicant, Lindmo et al. operates on unrelated and distinct principles which use non-colloidal particles.

In response to applicant's arguments against the Lindmo et al. and Grange et al. individually, one cannot show nonobviousness by attacking the references individually where the rejection is based on a combination of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, Lindmo et al. teach a reagent comprising a binary mixture of microparticles having two distinguishable microparticle types wherein each population has a mean diameter, distinguishable light scattering properties, i.e.

refractive index, and are coated with binding partners having the same specificity but different reactivity. Grange et al. is incorporated with the teaching of Lindmo, only for the teaching of a reagent comprising light scattering microparticles having a diameter of 300 nm for measurement at wavelengths of 220 to 600 nm. Sutton et al. is further incorporated herein, for disclosure of a microparticulate reagent having an oligonucleotide probe covalently attached thereto. It would have been obvious to one of ordinary skill in the art at the time of the instant invention to covalently attach oligonucleotide probes such as taught by Sutton into the microparticulate reagent taught by Lindmo as modified by Grange in order to create a reagent for detecting nucleic acid analytes because oligonucleotide probes constitute obvious variations of species of binding partners which are specific for nucleic acids and which are routinely varied in the art.

D) Applicant states that Collet-Cassart et al. discloses microparticles coated with anti-CRP antibodies that recognize different epitopes of the CRP protein for use in an agglutination assay to detect CRP. Applicant, however, argues that Collet-Cassart et al. fails to remedy the deficiency of the combined teaching of Lindmo et al. and Grange et al. since Lindmo et al. teaches away from the claimed invention for lack of teaching of agglutination assay applications and thus, is not combinable with the teaching of both Grange et al. and Collet-Cassart et al. According to Applicant, Lindmo et al. operates on unrelated and distinct principles which use non-colloidal particles.

In response to applicant's arguments against the Lindmo et al. and Grange et al. individually, one cannot show nonobviousness by attacking the references individually where the rejection is based on a combination of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, Lindmo et al. teach a reagent comprising a binary mixture of microparticles having two distinguishable microparticle types wherein each population has a mean diameter, distinguishable light scattering properties, i.e. refractive index, and are coated with binding partners having the same specificity but different reactivity. Grange et al. is incorporated with the teaching of Lindmo, only for the teaching of a reagent comprising light scattering microparticles having a diameter of 300 nm for measurement at wavelengths of 220 to 600 nm. Collet-Cassart et al. is further incorporated herein for the disclosure of microparticles coated with anti-CRP antibodies that recognize different epitopes of the CRP protein for use in an agglutination assay to detect CRP. It would have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute the anti-CRP antibodies in the reagent of Collet-Cassart for coating into the microparticulate reagent of Lindmo as modified by Grange because Lindmo specifically taught that it is well within ordinary skill to generate two groups of microparticles having distinct mean diameters coated with antibodies having distinct specificities, and Grange specifically taught that intensity of light scatter by a given suspension of microparticles in a reagent, when used in an agglutination assay is dependent on the size, i.e. 300 nm and number of the particles,

and Collet-Cassart specifically taught application of such agglutination assay for CRP using anti-CRP antibodies coated into microparticles.

E) Applicant states that Kapmeyer et al. disclose microparticles coated with monoclonal antibodies directed against different epitopes of PSA for use in an agglutination assay to detect PSA. Applicant, however, argues that Kapmeyer et al. fails to remedy the deficiency of the combined teaching of Lindmo et al. and Grange et al. since Lindmo et al. teaches away from the claimed invention for lack of teaching of agglutination assay applications and thus, is not combinable with the teaching of both Grange et al. and Kapmeyer et al. According to Applicant, Lindmo et al. operates on unrelated and distinct principles which use non-colloidal particles.

In response to applicant's arguments against the Lindmo et al. and Grange et al. individually, one cannot show nonobviousness by attacking the references individually where the rejection is based on a combination of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, Lindmo et al. teach a reagent comprising a binary mixture of microparticles having two distinguishable microparticle types wherein each population has a mean diameter, distinguishable light scattering properties, i.e. refractive index, and are coated with binding partners having the same specificity but different reactivity. Grange et al. is incorporated with the teaching of Lindmo, only for the teaching of a reagent comprising light scattering microparticles having a diameter of 300 nm for measurement at wavelengths of 220 to 600 nm. Kapmeyer et al. is further

incorporated herein for the disclosure of microparticles coated with monoclonal antibodies directed against different epitopes of PSA for use in an agglutination assay to detect PSA. It would have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute the anti-PSA monoclonal antibodies in the reagent of Kapmeyer for coating into the microparticulate reagent of Lindmo as modified by Grange because Lindmo specifically taught that it is well within ordinary skill to generate two groups of microparticles having distinct mean diameters coated with antibodies having distinct specificities, and Grange specifically taught that intensity of light scatter by a given suspension of microparticles in a reagent, when used in an agglutination assay is dependent on the size, i.e. 300 nm and number of the particles, and Kapmeyer specifically taught application of such agglutination assay for PSA using anti-PSA antibodies coated into microparticles.

7. No claims are allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday, Tuesday, and Thursday, 5:30 AM to 2:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-0169.

Gailene R. Gabel
Patent Examiner
Art Unit 1641
January 14, 2004

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641